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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,639	09/19/2001	Andrew L. Niles	34506.115	1780

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Intellectual Property Department  
DEWITT ROSS & STEVENS S.C.  
Firstar Financial Centre  
8000 Excelsior Drive, Suite 401  
Madison, WI 53717-1914

EXAMINER

CELSA, BENNETT M

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 03/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/955,639

Applicant(s)

NILES ET AL.

Examiner

Bennett Celsa

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/11/03.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-15, 28-37, 41, 42 and 44-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4-15 and 28-37 is/are allowed.
- 6) ☒ Claim(s) 41, 42 and 45 is/are rejected.
- 7) ☒ Claim(s) 44, 46 and 47 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12/11/03
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's amendment dated 12/11/03 is hereby acknowledged.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Status of the Claims***

Claims 4-15, 28-37, 41, 42 and 44-47 are currently pending and under consideration.

Claims 4-15 and 28-37, are allowable over the prior art of record.

Claims 44 and 46-47 are objected to as being dependent upon a rejected base claim.

Claims 41, 42 and 45 are rejected.

### ***Withdrawn Objection (s) and/or Rejection (s)***

Applicant's amendment has overcome the objection of claims 14 and 46 under 37 CFR 1.75(c), as being of improper dependent form.

In view of applicant's amendment, the prior 102(a,b) rejection over the Wei reference has been modified, and new rejections (e.g. 102/103 and 103 raised). These new rejections, necessitated by applicant's amendment, appear to address arguments presented by applicant already of record.

### ***New Objection (s) and/or Rejection (s)***

### ***Claim Rejections - 35 USC § 102/§103***

Claims 41, 42 and 45 are rejected under 35 U.S.C. 102(a,b) as being anticipated or in the alternative as being obvious over Wei et al. WO 98/50579 (11/98).

The presently claimed invention is directed to a kit for analyzing samples for beta-tryptase activity comprising a "suitable container" containing an isolated

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polypeptide comprising (amino to carboxyl) P4(PRO) – P3 (ala/arg/lys)-P2 (any amino acid)-P1 (lys/arg) wherein there is one detectable leaving group covalently bound (Claim 41). The isolated polypeptide can be in solution, lyophilized or bound to a solid support (claim 42) . The detectable leaving group could be fluorogenic and bounded to a carboxy terminus of P4-P3-P2-P1 (claim 45).

Wei et al. teach fluorogenic protease substrates and kits (e.g. containers) thereof (e.g see page 2) which comprise the sequence Val-Pro-Arg-Gly-Lys (e.g. in solution see page 9; and examples and claims) which is within the scope of the presently claimed invention where: P4-P3-P2-P1 is Pro-Arg-Gly-Lys and Pro . It is noted that in a compound/composition claim intended use language (e. g. “for analyzing samples for Beta-tryptase activity” ) is not afforded patentable weight; and in any event the Wei reference teaches that Val-Pro-Arg-Gly-Lys can (and is ) used as a tryptase substrate.

Wei et al. Example 1, although teaching a dual labeled fluorogenic substrate clearly teaches the making of a single-labeled counterpart which would anticipate the covalent attachment of one detectable (e.g. fluorogenic) leaving group to an isolated polypeptide comprising P4-P3-P2-P1: “This dual-labeled conjugate shown below, exhibited substantially lower fluorescence **than its singly labeled counterpart (emphasis provided); which would encompass a fluorescent group at the amino or carboxyl terminus of the Example 1 peptide .** Accordingly, with regard to present claim 45, the Wei reference would anticipate, or in the alternative render obvious the making of a peptide comprising P4-P3-P2-P1 with a carboxy fluorogenic

group since the reference teaches making a single labeled counterpart which encompasses only 2 possible species e.g. fluorogenic attachment at the N or C terminus. See *In re Schaumann*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978).

Additionally, the Wei reference teaches the use of "fluorescence dye quenching" as well as "dimerization or dye stacking" (e.g. see Wei at pages 3-4) utilized in Example 1, as an alternative means of assay to which the "singly labeled counterpart" would be applicable.

Claims 41, 42 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wei et al. WO 98/50579 (11/98) and Yaron et al. US Pat. No. 4,314,936 (2/82).

The presently claimed invention is directed to a kit for analyzing samples for beta-tryptase activity comprising a "suitable container" containing an isolated polypeptide comprising (amino to carboxyl) P4(PRO) – P3 (ala/arg/lys)-P2 (any amino acid)-P1 (lys/arg) wherein there is one detectable leaving group covalently bound (Claim 41). The isolated polypeptide can be in solution, lyophilized or bound to a solid support (claim 42). The detectable leaving group could be fluorogenic and bounded to a carboxy terminus of P4-P3-P2-P1 (claim 45).

Wei et al. teach fluorogenic protease substrates and kits (e.g. containers) thereof (e.g. see page 2) which comprise the sequence Val-Pro-Arg-Gly-Lys (e.g. in solution see page 9; and examples and claims) which is within the scope of the presently claimed invention where: P4-P3-P2-P1 is Pro-Arg-Gly-Lys and Pro. It is noted that in a compound/composition claim intended use language (e. g. "for analyzing

samples for Beta-tryptase activity” ) is not afforded patentable weight; and in any event the reference teaches that Val-Pro-Arg-Gly-Lys can (and is ) used as a tryptase substrate.

Wei et al. Example 1, although teaching a dual labeled fluorogenic substrate, clearly teaches the making of a single-labeled counterpart which would anticipate the covalent attachment of one detectable (e.g. fluorogenic) leaving group to an isolated polypeptide comprising P4-P3-P2-P1: “This dual-labeled conjugate shown below, exhibited substantially lower fluorescence **than its singly labeled counterpart (emphasis provided); which would encompass a fluorescent group at the amino or carboxyl terminus of the Example 1 peptide.** Accordingly, with regard to present claim 45, the Wei reference would anticipate, or in the alternative render obvious the making of a P4-P3-P2-P1 with a carboxy fluorogenic group since the reference teaches making a single labeled counterpart which encompasses only 2 possible species e.g. fluorogenic attachment at the N or C terminus. See *In re Schaumann*, 572 F.2d 312. 197 USPQ 5 (CCPA 1978).

Alternatively, the Wei reference teaches the use of “fluorescence dye quenching” as well as “dimerization or dye stacking” (e.g. see Wei at pages 3-4) utilized in Example 1, as an alternative means of assay to which the “singly labeled counterpart” would be applicable. For example, the Wei reference (cited in the Yaron et al. patent at page 3), teaches the favorable (e.g. efficient and sensitive: see col. 1 of Yaron) use of fluorescence dye quenching assays of protease peptide hydrolases,

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including trypsin-like peptidyl peptide hydrolases (e.g. see col. 1-2; formulas 1-6 and especially formulas 5-6).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize kits comprising containers containing singly labeled polypeptides comprising P4-P3-P2-P1 polypeptides as disclosed in the Wei reference (e.g. see example 1) in a fluorescent dye quenching assay as taught by the Yaron et al. patent since:

the Wei reference specifically teaches the equivalent use of kits containing protease (e.g. trypsin substrates) in both fluorescent dye quenching assays and dimer stacking assays; and/or the Wei reference specifically points to the Yaron et al. patent which teaches the benefits of using fluoresceine dye quenching (e.g. efficient and sensitive).

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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***Future Correspondences***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-273-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa  
Primary Examiner  
Art Unit 1639

BC  
March 9, 2004